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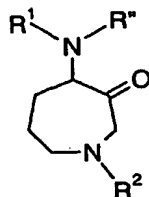
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- (21) International Application Number: **PCT/US2003/026358** (74) Agents: **KANAGY, James, M. et al.; SmithKline Beecham Corporation, Corporate Intellectual Property, UW2220, 709 Swedeland Road, P.O. Box 1539, King of Prussia, PA 19406-0939 (US).**
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- Published:**  
— *without international search report and to be republished upon receipt of that report*
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

(54) Title: **PROTEASE INHIBITORS**



(1)

(57) Abstract: This invention relates 4-amino-azepan-3-ones of formula (1) which are useful as protease inhibitors, particularly of cathepsin S, and as such are useful for preventing a number of diseases amongst which are atherosclerotic lesions and pulmonary diseases such as asthma and allergic reactions.

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# PATENT COOPERATION TREATY

## PCT

### INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Rec'd PCT/PTC 18 FEB 2005

REC'D 03 JAN 2005

WIPO PCT

Applicant's or agent's file reference <b>P51371</b>	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. <b>PCT/US03/26358</b>	International filing date (day/month/year) <b>22 August 2003 (22.08.2003)</b>	Priority date (day/month/year) <b>22 August 2002 (22.08.2002)</b>
International Patent Classification (IPC) or national classification and IPC <b>IPC(7): A61K 31/55; A61P 31/00; C07D 223/08, 401/00, 403/00, 405/00, 413/00, 415/00, 417/00, 419/00 and US Cl.: 514/217.03, 217.04, 217.05, 217.06, 217.07, 217.08, 217.09, 217.10, 217.11; 540/596, 597, 598, 599</b>		
Applicant <b>SMITHKLINE BEECHAM CORPORATION</b>		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 4 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of \_\_\_ sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of report with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand <b>30 January 2004 (30.01.2004)</b>	Date of completion of this report <b>12 December 2004 (12.12.2004)</b>
Name and mailing address of the IPEA/US Mail Stop PCT, Attn: IPEA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Authorized officer <b>Brenda Coleman</b> Telephone No. 571-272-1600

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US03/26358

## I. Basis of the report

### 1. With regard to the elements of the international application:\*

- ☒ the international application as originally filed.
- ☒ the description:  
 pages 1-70 \_\_\_\_\_ as originally filed  
 pages NONE \_\_\_\_\_, filed with the demand  
 pages NONE \_\_\_\_\_, filed with the letter of \_\_\_\_\_.
- ☒ the claims:  
 pages 71-82 \_\_\_\_\_, as originally filed  
 pages NONE \_\_\_\_\_, as amended (together with any statement) under Article 19  
 pages NONE \_\_\_\_\_, filed with the demand  
 pages NONE \_\_\_\_\_, filed with the letter of \_\_\_\_\_.
- ☐ the drawings:  
 pages NONE \_\_\_\_\_, as originally filed  
 pages NONE \_\_\_\_\_, filed with the demand  
 pages NONE \_\_\_\_\_, filed with the letter of \_\_\_\_\_.
- ☐ the sequence listing part of the description:  
 pages NONE \_\_\_\_\_, as originally filed  
 pages NONE \_\_\_\_\_, filed with the demand  
 pages NONE \_\_\_\_\_, filed with the letter of \_\_\_\_\_.

### 2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language \_\_\_\_\_ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

### 3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in printed form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

### 4. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages NONE
- ☐ the claims, Nos. NONE
- ☐ the drawings, sheets/~~fig~~ NONE

### 5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).\*\*

\* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

\*\* Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

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III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The question whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been and will not be examined in respect of:

☐ the entire international application,

☒ claims Nos. 4

because:

☐ the said international application, or the said claim Nos. \_\_\_\_\_ relate to the following subject matter which does not require international preliminary examination (*specify*):

☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 4 are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. \_\_\_\_\_ are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for said claims Nos. \_\_\_\_\_

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.  
PCT/US03/26358

## V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

### 1. STATEMENT

Novelty (N)	Claims <u>NONE</u>	<u>YES</u>
	Claims <u>1-3 and 5-10</u>	<u>NO</u>
Inventive Step (IS)	Claims <u>NONE</u>	<u>YES</u>
	Claims <u>1-3 and 5-10</u>	<u>NO</u>
Industrial Applicability (IA)	Claims <u>1-3 and 5-10</u>	<u>YES</u>
	Claims <u>NONE</u>	<u>NO</u>

### 2. CITATIONS AND EXPLANATIONS

Claims 1-3 and 5-10 lack novelty under PCT Article 33(2) as being anticipated by SMITHKLINE BEECHAM CORPORATION, WO 01/89451. SMITHKLINE BEECHAM CORPORATION teaches the compounds of formula II and method of use of the compounds of formula I where R<sup>2</sup> is -SO<sub>2</sub>-pyridin-2-yl, n-propyl, etc.; R''' is H, methyl, etc.; R'' is H; and R<sup>1</sup> is -C(=O)-CH(i-Bu)-N(R')(R<sup>4</sup>), -C(=O)-CH(cyclohexylmethyl)-N(R')(R<sup>4</sup>), -C(=O)-CH(t-Bu)-N(R')(R<sup>4</sup>), etc.

Claims 1-3 and 5-10 lack an inventive step under PCT Article 33(3) as being obvious over SMITHKLINE BEECHAM CORPORATION, WO 01/89451. For reasons stated above.

Claims 1-3 and 5-10 meet the criteria set out in PCT Article 33(4), and thus the compounds and method of use of the compounds of formula I have industrial applicability because the subject matter claimed can be made or used in industry.